

Under the Paperwork Reduction Act of 1995, no person is required to respond to a collection of information unless it contains a valid OMB control number

Substitute for Form 1449/A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Complete if Known

| | |
|------------------------|---------------------------|
| Application No. | 10/077,142 |
| Filing Date | 02/15/2002 |
| First Named Inventor | D'Amato et al. |
| Group Art Unit | 1616 |
| Examiner Name | Badio, Barbara P. |
| Attorney Docket Number | 05213-3000 (43170-269288) |

Sheet 1 of 15

U.S. PATENT DOCUMENTS

| Examiner Initials | Cite No. ¹ | U.S. Patent Document | | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
|----------------------|--------------------------|----------------------|--------------------------------------|--|--|---|
| | | Number ² | Kind Code ³ (if known) | | | |
| | 1 | 3,166,577 | | Ringold et al. | 01/19/1965 | |
| | 2 | 3,562,260 | | De Ruggieri et al. | 02/09/1971 | |
| | 3 | 4,552,758 | | Murphy et al. | 11/12/1985 | |
| | 4 | 4,808,402 | | Leibovich et al. | 02/28/1989 | |

Examiner
SignatureDate
Considered

¹Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language translation is attached.

Under the Paperwork Reduction Act of 1995, no person is required to respond to a collection of information unless it contains a valid OMB control number

Substitute for Form 1449/A/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Complete if Known

| | |
|------------------------|---------------------------|
| Application No. | 10/077,142 |
| Filing Date | 02/15/2002 |
| First Named Inventor | D'Amato et al. |
| Group Art Unit | 1616 |
| Examiner Name | Badio, Barbara P. |
| Attorney Docket Number | 05213-3000 (43170-269288) |

Sheet 2 of 15

FOREIGN PATENT DOCUMENTS

| Examiner Initials | Cite No. ¹ | Foreign Patent Document | | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear | T ² |
|----------------------|--------------------------|-------------------------|---------------------|--|--|---|----------------|
| | | Office ³ | Number ⁴ | Kind Code ⁵ (if known) | | | |
| | 5 | WO | 88/08002 | A1 | The Upjohn Company | 10/20/1988 | |
| | 6 | WO | 93/19746 | A1 | ORION-YH-TYMA OY | 10/14/1993 | |

Examiner
SignatureDate
Considered

¹Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language translation is attached.

Under the Paperwork Reduction Act of 1995, respondents are required to respond to a collection of information unless it contains a valid OMB control number

| | | | | | |
|---|-----------------------|--|----|-------------------|--|
| Substitute for Form 1449/A/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary) | | | | Complete if Known | |
| | | | | Application No. | 10/077,142 |
| Sheet | | 3 | of | 15 | Filing Date 02/15/2002 First Named Inventor D'Amato et al. Group Art Unit 1616 Examiner Name Badio, Barbara P. Attorney Docket Number 05213-3000 (43170-269288) |
| OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS | | | | | |
| Examiner Initials | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published | | | T* |
| | 7 | Author: Title: Publi: Research Plus Catalog Vol/Iss: Pages: 50-58 Date: 1993 | | | |
| | 8 | Author: Title: Registry Number: 56933-77-8 Publi: Chemical Abstracts Vol/Iss: Pages: Date: | | | |
| | 9 | Author: Title: Registry Number: 56933-78-9 Publi: Chemical Abstracts Vol/Iss: Pages: Date: | | | |
| | 10 | Author: Title: Registry Number: 57380-15-1 Publi: Chemical Abstracts Vol/Iss: Pages: Date: | | | |
| | 11 | Author: Title: Registry Number: 71782-94-0 Publi: Chemical Abstracts Vol/Iss: Pages: Date: | | | |
| | 12 | Author: Title: Registry Number: 71782-95-1 Publi: Chemical Abstracts Vol/Iss: Pages: Date: | | | |
| | 13 | Author: Title: Registry Number: 101277-11-6 Publi: Chemical Abstracts Vol/Iss: Pages: Date: | | | |

| | |
|--------------------|-----------------|
| Examiner Signature | Date Considered |
|--------------------|-----------------|

¹Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language translation is attached.

RECEIVED
TECH CENTER
DEC 08 2003
1600/2900

Under the Paperwork Reduction Act of 1995, no person is required to respond to a collection of information unless it contains a valid OMB control number

| | | | | | |
|---|----------|---|----|------------------------|---------------------------|
| Substitute for Form 1449/A/PTO | | | | Complete if Known | |
| INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary) | | | | Application No. | 10/077,142 |
| | | | | Filing Date | 02/15/2002 |
| | | | | First Named Inventor | D'Amato et al. |
| | | | | Group Art Unit | 1616 |
| | | | | Examiner Name | Badio, Barbara P. |
| Sheet | 4 | of | 15 | Attorney Docket Number | 05213-3000 (43170-269288) |
| OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS | | | | | |
| Examiner Initials | Cite No. | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published | | | T* |
| | 14 | Author: Title: Registry Number: 101429-40-7 Publ: Chemical Abstracts Vol/Iss: Pages: Date: | | | |
| | 15 | Author: Title: Registry Number: 162853-20-5 Publ: Chemical Abstracts Vol/Iss: Pages: Date: | | | |
| | 16 | Author: ABOULWafa et al. Title: Synthesis and evaluation for uterotrophic and antiimplantation activities of 2-substituted estradiol derivatives Publ: Steroids Vol/Iss: 57 Pages: 199-204 Date: 04/1992 | | | |
| | 17 | Author: ALGIRE, G.H. et al. Title: Vascular reactions of normal and malignant tumors in vivo. I. Vascular reactions of mice to wounds and to normal and neoplastic transplants Publ: Journal of the National Cancer Institute Vol/Iss: 6 Pages: 73-85 Date: 08/1945 | | | |
| | 18 | Author: ALIEV et al. Title: 54929q Synthesis of cycloalkyl derivatives of dihydric phenols and their ethers Publ: Chemical Abstracts Vol/Iss: 72 Pages: 370 Date: 1970 | | | |
| | 19 | Author: BARNES et al. Title: Tumor Necrosis Factor Production in Patients with Leprosy Publ: Infection and Immunity Vol/Iss: 60 (4) Pages: 1441-1446 Date: 04/1992 | | | |
| | 20 | Author: BINDRA et al. Title: Studies in Antifertility Agents. 8. Seco Steroids. 2. 5,6-Secoestradiol and Some Related Compounds Publ: Journal of Medicinal Chemistry Vol/Iss: 18 (9) Pages: 921-925 Date: 1975 | | | |

| | | | |
|--------------------|--|-----------------|--|
| Examiner Signature | | Date Considered | |
|--------------------|--|-----------------|--|

*Unique citation designation number. *See attached Kinds of U.S. Patent Documents. *Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). *For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. *Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. *Applicant is to place a check mark here if English language translation is attached.

RECEIVED
TECH CENTER
DEC 05 2003
1600/2900

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

| | | | | | |
|---|----------|--|----|------------------------|---------------------------|
| Substitute for Form 1449/A/PTO | | | | Complete if Known | |
| INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary) | | | | Application No. | 10/077,142 |
| | | | | Filing Date | 02/15/2002 |
| | | | | First Named Inventor | D'Amato et al. |
| | | | | Group Art Unit | 1616 |
| | | | | Examiner Name | Badio, Barbara P. |
| Sheet | 5 | of | 15 | Attorney Docket Number | 05213-3000 (43170-269288) |
| OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS | | | | | |
| Examiner Initials | Cite No. | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published | | | T* |
| | 21 | Author: BLICKENSTAFF et al. Title: SYNTHESIS OF SOME ANALOGS OF ESTRADIOL Publ: Steroids Vol/Iss: 46 (4,5) Pages: 889-902 Date: 10/1985 | | | |
| | 22 | Author: BOYCE et al. Title: Some Preliminary Synthetical Studies with 5,6,7,8-Tetra-hydro-8-methylindane -1,5-dione Publ: Unknown Vol/Iss: Pages: 4547-4553 Date: 1960 | | | |
| | 23 | Author: BRANDI et al. Title: Bone endothelial cells as estrogen targets (Abstract only) Publ: Calcif. Tissue Int. Vol/Iss: 53 (5) Pages: 312-317 Date: 1993 | | | |
| | 24 | Author: BREM, H. et al. Title: Interstitial chemotherapy with drug polymer implants for the treatment of recurrent gliomas Publ: Journal of Neurosurgery Vol/Iss: 74 Pages: 441-446 Date: 03/01/91 | | | |
| | 25 | Author: CAMBIE et al. Title: Aromatic Steroids. Part I. Oxidation Products of 3-Methoxyestra-1,3,5(10)-triene-17 β -yl Acetate Publ: J. Chem. Soc. Vol/Iss: Pages: 2603-2608 Date: 1968 | | | |
| | 26 | Author: COREY et al. Title: Applications of N,N-Dimethylhydrazones to Synthesis. Use in Efficient, Positionally and Stereochemically Selective C-C Bond Formation; Oxidative Hydrolysis to Carbonyl Compounds Publ: Tetrahedron Letters Vol/Iss: 1 Pages: 3-6 Date: 1976 | | | |
| | 27 | Author: COREY et al. Title: Facile Conversion of N,N-Dimethylhydrazones to Carbonyl Compounds by Cupric Ion-Catalyzed Hydrolysis Publ: Tetrahedron Letters Vol/Iss: 41 Pages: 36678-3668 Date: 1976 | | | |

| | | | |
|--------------------|--|-----------------|--|
| Examiner Signature | | Date Considered | |
|--------------------|--|-----------------|--|

*Unique citation designation number. *See attached Kinds of U.S. Patent Documents. *Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). *For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. *Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. *Applicant is to place a check mark here if English language translation is attached.

| | | | | | |
|---|-----------------------|--|--|------------------------|---------------------------|
| Substitute for Form 1449/A/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary) | | | | Complete if Known | |
| | | | | Application No. | 10/077,142 |
| | | | | Filing Date | 02/15/2002 |
| | | | | First Named Inventor | D'Amato et al. |
| | | | | Group Art Unit | 1616 |
| Sheet 6 of 15 | | | | Examiner Name | Badlo, Barbara P. |
| | | | | Attorney Docket Number | 05213-3000 (43170-269288) |
| OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS | | | | | |
| Examiner Initials | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published | | | T* |
| | 28 | Author: CRABBE, P. Title: Cotton effect of the styrene chromophore (Abstract only) Publ: Chem. Ind. Vol/Iss: 27 Pages: 917-918 Date: 1969 | | | |
| | 29 | Author: DURANI et al. Title: Seco-Oestradiols and Some Non-Steroidal Oestrogens: Structural Correlates of Oestrogenic Action Publ: Journal of Steroid Biochemistry Vol/Iss: 11 Pages: 67-77 Date: 1979 | | | |
| | 30 | Author: EDER et al. Title: Synthese von Ostradiol (in German - No translation available) Publ: Chem. Ber. Vol/Iss: 109 Pages: 2948-2953 Date: 1976 | | | |
| | 31 | Author: EMONS et al. Title: Modulation der hypophysären Sekretion von Luteinisierendem Hormon (LH) durch Östrogene Publ: FOCUS MHL Vol/Iss: 3 Pages: 221-228 Date: 1986 | | | |
| | 32 | Author: FANCHENKO et al. Title: Characteristics of the guinea pig uterus estrogen receptor system (Abstract only) Publ: Byull. Eksp. Biol. Med. Vol/Iss: 85 (4) Pages: 467-470 Date: 1978 | | | |
| | 33 | Author: FEVIG et al. Title: A Short, Stereoselective Route to 16 α -(Substituted-alkyl)estradiol Derivatives Publ: Journal of Organic Chemistry Vol/Iss: 52 Pages: 247-251 Date: 1987 | | | |
| | 34 | Author: FIELD et al. Title: Effect of Thalidomide on the Graft versus Host Reaction Publ: Nature Vol/Iss: 211 (5055) Pages: 1308-1310 Date: 09/17/66 | | | |

| | |
|--------------------|-----------------|
| Examiner Signature | Date Considered |
|--------------------|-----------------|

¹Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language translation is attached.

Substitute for Form 1449/A/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet

15

of

15

Complete if Known

| | |
|------------------------|---------------------------|
| Application No. | 10/077,142 |
| Filing Date | 02/15/2002 |
| First Named Inventor | D'Amato et al. |
| Group Art Unit | 1616 |
| Examiner Name | Badio, Barbara P. |
| Attorney Docket Number | 05213-3000 (43170-269288) |

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

| Examiner Initials | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published | T ² |
|-------------------|-----------------------|--|----------------|
| | 91 | Author: VICENTE et al. Title: In Vitro Activity of Thalidomide Against Mycobacterium avium Complex Publ: Archives of Internal Medicine Vol/Iss: 153 (4) Pages: 534 Date: 02/22/93 | |
| | 92 | Author: WANG et al. Title: Photoaffinity labeling of human placental estradiol 17.β-dehydrogenase with 2- and 4-azidoestrone, 2- and 4-azidoestradiol (Abstract only) Publ: Shengwu Huaxue Zazhi Vol/Iss: 8 (6) Pages: 715-718 Date: 1992 | |
| | 93 | Author: WEIDNER, N. et al. Title: Tumor angiogenesis: A New Significant and Independent Prognostic Indicator in Early-Stage Breast Carcinoma Publ: Journal of the National Cancer Institute Vol/Iss: 84 Pages: 1875-1887 Date: 12/16/92 | |
| | 94 | Author: WEIDNER, N. et al. Title: Tumor Angiogenesis Correlates with Metastasis in Invasive Prostate Carcinoma Publ: American Journal of Pathology Vol/Iss: 143 (2) Pages: 401-409 Date: 08/1993 | |
| | 95 | Author: WEIDNER, N. et al. Title: Tumor Angiogenesis and Metastasis-Correlation in Invasive Breast Carcinoma Publ: New England Journal of Medicine Vol/Iss: 324 (1) Pages: 1-8 Date: 01/03/91 | |
| | 96 | Author: WELSCH et al. Title: Staphylostatic Activity of Some New Diphenols, Naphthols, and Chalcones (Abstract only) Publ: Experientia Vol/Iss: 11 Pages: 350-351 Date: 1955 | |
| | 97 | Author: WHITE et al. Title: Treatment of Pulmonary Hemangiomas with Recombinant Interferon Alfa-2a Publ: The New England Journal of Medicine Vol/Iss: 32 (18) Pages: 1197-1200 Date: 05/04/89 | |

Examiner
SignatureDate
Considered

¹Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language translation is attached.

Substitute for Form 1449/A/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet 13 of 15

Complete if Known

| | |
|------------------------|---------------------------|
| Application No. | 10/077,142 |
| Filing Date | 02/15/2002 |
| First Named Inventor | D'Amato et al. |
| Group Art Unit | 1616 |
| Examiner Name | Badio, Barbara P. |
| Attorney Docket Number | 05213-3000 (43170-269288) |

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

| Examiner Initials | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published | T |
|-------------------|-----------------------|---|---|
| | 77 | Author: NEWKOME et al. Title: Synthesis of Simple Hydrazones of Carbonyl Compounds by an Exchange Reaction Publ: Journal of Organic Chemistry Vol/Iss: 31 Pages: 677-681 Date: 03/1966 | |
| | 78 | Author: NGUYEN, M. et al. Title: Elevated Levels of the Angiogenic Peptide Basic Fibroblast Growth Factor in Urine of Bladder Cancer Patients Publ: Journal of the National Cancer Institute Vol/Iss: 85 (3) Pages: 241-242 Date: 02/03/93 | |
| | 79 | Author: NUMAZAWA et al. Title: Novel and Regiospecific Synthesis of 2-Amino Estrogens via Zincke Nitration Publ: Steroids Vol/Iss: 41 (5) Pages: 675-682 Date: 1983 | |
| | 80 | Author: PERT et al. Title: Preparations of 2,4-disubstituted estradiols (Abstract only) Publ: Australian Journal of Chemistry Vol/Iss: 42 (3) Pages: 421-432 Date: 1989 | |
| | 81 | Author: PETERS et al. Title: 17-Desoxy Estrogen Analogues Publ: Journal of Medicinal Chemistry Vol/Iss: 32 (7) Pages: 1642-1652 Date: 1989 | |
| | 82 | Author: PFEIFFER et al. Title: Are catechol estrogens obligatory mediators of estrogen action in the central nervous system? I. Characterization of pharmacological probes with different receptor binding affinities and catechol estrogen formation rates (Abstract only) Publ: Journal of Endocrinology Vol/Iss: 110 (3) Pages: 489-497 Date: 1986 | |
| | 83 | Author: POWELL et al. Title: Investigation and Treatment of Orogenital Ulceration; studies on a Possible Mode of Action of Thalidomide Publ: British Journal of Dermatology Vol/Iss: 113 Supp. 28 Pages: 141-144 Date: 07/1985 | |

| | |
|--------------------|-----------------|
| Examiner Signature | Date Considered |
|--------------------|-----------------|

¹Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language translation is attached.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

| | | | | | |
|---|-----------------------|--|--|------------------------|---------------------------|
| Substitute for Form 1449/A/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary) | | | | Complete if Known | |
| | | | | Application No. | 10/077,142 |
| | | | | Filing Date | 02/15/2002 |
| | | | | First Named Inventor | D'Amato et al. |
| | | | | Group Art Unit | 1616 |
| Sheet 14 of 15 | | | | Examiner Name | Badio, Barbara P. |
| | | | | Attorney Docket Number | 05213-3000 (43170-269288) |
| OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS | | | | | |
| Examiner Initials | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published | | | T ² |
| | 84 | Author: SHISHKINA et al. Title: Synthesis and properties of condensed heterocyclic derivatives of estra-4, 9-dien-17. beta.-ol-3-one (Abstract only) Publ: Khim.-Farm. Zh. Vol/Iss: 8 (1) Pages: 7-11 Date: 1974 | | | |
| | 85 | Author: SIDKY et al. Title: Inhibition of Angiogenesis by Interferons: Effects on Tumor- and Lymphocyte-induced Vascular Responses Publ: Cancer Research Vol/Iss: 47 Pages: 5155-5161 Date: 10/01/87 | | | |
| | 86 | Author: SIRACUSA et al. Title: The effect of microtubule- and microfilament-disrupting drugs on preimplantation mouse embryos (Abstract only) Publ: Journal of Embryology and Experimental Morphology Vol/Iss: 60 Pages: 71-82 Date: 12/1980 | | | |
| | 87 | Author: SPYRIOUNIS et al. Title: Copper (II) complex of an estradiol derivative with potent antiinflammatory properties (Abstract only) Publ: Arch. Pharm. Vol/Iss: 324 (9) Pages: 533-536 Date: 1991 | | | |
| | 88 | Author: SRIVASTAVA, A. et al. Title: The Prognostic Significance of Tumor Vascularity in Intermediate-Thickness (0.76-4.0 mm Thick) Skin Melanoma Publ: American Journal of Pathology Vol/Iss: 133 (2) Pages: 419-424 Date: 11/1988 | | | |
| | 89 | Author: STARKOV et al. Title: Mono- and Dialkylation of Guaiacol by Olefins on KU-2 Cation Exchanger (Abstract only) Publ: Zhurnal Prikladnoi Khimii Vol/Iss: 41 (3) Pages: 688-690 Date: 1968 | | | |
| | 90 | Author: TAYLOR, S. et al. Title: Protamine is an Inhibitor of Angiogenesis Publ: Nature Vol/Iss: 297 Pages: 307-312 Date: 05/27/82 | | | |

| | |
|--------------------|-----------------|
| Examiner Signature | Date Considered |
|--------------------|-----------------|

¹Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language translation is attached.

Substitute for Form 1449/A/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet 12 of 15

Complete if Known

| | |
|------------------------|---------------------------|
| Application No. | 10/077,142 |
| Filing Date | 02/15/2002 |
| First Named Inventor | D'Amato et al. |
| Group Art Unit | 1616 |
| Examiner Name | Badio, Barbara P. |
| Attorney Docket Number | 05213-3000 (43170-269288) |

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

| Examiner Initials | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published | T ² |
|-------------------|-----------------------|--|----------------|
| | 70 | Author: LOOZEN et al. Title: An approach to the synthesis of 7.beta.-amino estrogens (Abstract only) Publ: Recl.: J.R. Neth.Chem. Soc. Vol/Iss: 102 (10) Pages: 433-437 Date: 1983 | |
| | 71 | Author: MARO et al. Title: Mechanism of Polar Body Formation in the Mouse Oocyte: An Interaction Between the Chromosomes, the Cytoskeleton and the Plasma Membrane Publ: Journal of Embryology and Experimental Morphology Vol/Iss: 92 Pages: 11-32 Date: 1986 | |
| | 72 | Author: MICHEL et al. Title: Inhibition of synaptosomal high-affinity uptake of dopamine and serotonin by estrogen agonists and antagonists (Abstract only) Publ: Biochem. Pharmacol. Vol/Iss: 36 (19) Pages: 3175-3180 Date: 1987 | |
| | 73 | Author: MORISAKI et al. Title: Steroids. LI. Aromatization reaction of the cross-conjugated dienone system by Zinc 9. (Abstract only) Publ: Chem. Pharm. Bull. Vol/Iss: 14 (8) Pages: 866-872 Date: 1966 | |
| | 74 | Author: NAAFS et al. Title: Thalidomide Therapy An Open Trial Publ: International Journal of Dermatology Vol/Iss: 24 (2) Pages: 131-134 Date: 03/1985 | |
| | 75 | Author: NAMBARA et al. Title: Microbial transformation products derived from steroids. I. Synthesis of 1,2- and 3-dimethoxy-4-methylestratrienes (Abstract only) Publ: Chem. Pharm. Bull. Vol/Iss: 20 (2) Pages: 336-342 Date: 1972 | |
| | 76 | Author: NAMBARA et al. Title: Synthesis of 16β-Oxygenated Catechol Estrogen Methyl Ethers, New and Potential Metabolites Publ: Chemical & Pharmaceutical Bulletin Vol/Iss: 23 (7) Pages: 1613-1616 Date: 07/1975 | |

Examiner
SignatureDate
Considered

¹Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language translation is attached.

Under the Paperwork Reduction Act of 1996, no persons are required to respond to a collection of information unless it contains a valid OMB control number

| | | | | | |
|---|--------------------------|---|----|------------------------|---------------------------|
| Substitute for Form 1449/A/PTO | | | | Complete if Known | |
| INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary) | | | | Application No. | 10/077,142 |
| | | | | Filing Date | 02/15/2002 |
| | | | | First Named Inventor | D'Amato et al. |
| | | | | Group Art Unit | 1616 |
| | | | | Examiner Name | Badio, Barbara P. |
| Sheet | 11 | of | 15 | Attorney Docket Number | 05213-3000 (43170-269288) |
| OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS | | | | | |
| Examiner Initials | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published | | | T ² |
| | 63 | Author: KNIGHTON, D. et al. Title: Avascular and Vascular Phases of Tumour Growth in the Chick Embryo Publ: British Journal of Cancer Vol/Iss: 35 Pages: 347-356 Date: 1977 | | | |
| | 64 | Author: KOLÉ et al. Title: Studies in Antifertility Agents. 11. Secosteroids. 5. Synthesis of 9,11-Secoestradiol Publ: Journal of Medicinal Chemistry Vol/Iss: 18 (7) Pages: 765-766 Date: 1975 | | | |
| | 65 | Author: KOVACS et al. Title: Steroids. XXIII. Synthesis of 2- and 4-hydroxy and 2,4-dihydroxy derivatives of estrone and estradiol (Abstract only) Publ: Acta Phys. Chem. Vol/Iss: 19 (3) Pages: 287-290 Date: 1973 | | | |
| | 66 | Author: LEWIS, Richard J. Title: Publ: Hawley's Condensed Chemical Dictionary Vol/Iss: Pages: 577 Date: 01/1993 | | | |
| | 67 | Author: LEWIS, Richard J. Title: Publ: Hawley's Condensed Chemical Dictionary Vol/Iss: Pages: 128-129 Date: 01/1993 | | | |
| | 68 | Author: LIEN, W. et al. Title: The blood supply of experimental liver metastases. II. A Microcirculatory study of the normal and tumor vessels of the liver with the use of perfused silicone rubber Publ: Surgery Vol/Iss: 68 (2) Pages: 334-340 Date: 08/1970 | | | |
| | 69 | Author: LIU et al. Title: Total Synthesis of (+-) - $\Delta^{8(12)}$ Capnellene Publ: Tetrahedron Letters Vol/Iss: 26 (40) Pages: 4847-4850 Date: 1985 | | | |

| | |
|-----------------------|--------------------|
| Examiner Signature | Date Considered |
|-----------------------|--------------------|

¹Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language translation is attached.

| | | | | | |
|---|----------|--|----|------------------------|---------------------------|
| Substitute for Form 1449/A/PTO | | | | Complete if Known | |
| INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary) | | | | Application No. | 10/077,142 |
| | | | | Filing Date | 02/15/2002 |
| | | | | First Named Inventor | D'Amato et al. |
| | | | | Group Art Unit | 1616 |
| | | | | Examiner Name | Badio, Barbara P. |
| Sheet | 7 | of | 15 | Attorney Docket Number | 05213-3000 (43170-269288) |
| OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS | | | | | |
| Examiner Initials | Cite No. | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published | | | T* |
| | 35 | Author: FIESER et al. Title: N-Methylformanilide Publi: Organic Synthesis Collective Volume 3 Vol/Iss: 3 Pages: 590-591 Date: 1955 | | | |
| | 36 | Author: FLOHE et al. Title: Studies on the Hypothetical Relationship of Thalidomide-induced Embryopathy and Collagen Biosynthesis Publi: Arzneimitte/Forschung (Germany West) Vol/Iss: 31 (2) Pages: 315-320 Date: 01/01/81 | | | |
| | 37 | Author: FOLKMAN et al. Title: Angiogenesis Inhibition and Tumor Regression Caused by Heparin or a Heparin Fragment in the Presence of Cortisone Publi: Science Vol/Iss: 221 Pages: 719-725 Date: 08/19/83 | | | |
| | 38 | Author: FOLKMAN, J. Title: Tumor Angiogenesis: Therapeutic Implications Publi: New England Journal of Medicine Vol/Iss: 285 (21) Pages: 1182-1186 Date: 11/18/71 | | | |
| | 39 | Author: FOLKMAN, J. et al. Title: Induction of Angiogenesis During the Transition from Hyperplasia to Neoplasia Publi: Nature Vol/Iss: 339 Pages: 58-61 Date: 05/04/89 | | | |
| | 40 | Author: FOLKMAN, J. et al. Title: Tumor Behavior in Isolated Perfused Organs in vitro Growth and Metastases of Biopsy Material in Rabbit Thyroid and Canine Intestinal Segment Publi: Annals of Surgery Vol/Iss: 164(3) Pages: 491-502 Date: 09/01/66 | | | |
| | 41 | Author: GANDHI et al. Title: Mannich reaction of estrone Publi: Journal of Indian Chem. Soc. Vol/Iss: 39 Pages: 306-308 Date: 1962 | | | |

| | |
|--------------------|-----------------|
| Examiner Signature | Date Considered |
|--------------------|-----------------|

*Unique citation designation number. *See attached Kinds of U.S. Patent Documents. *Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). *For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. *Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. *Applicant is to place a check mark here if English language translation is attached.

| | | | | | |
|---|-----------------------|---|--|------------------------|---------------------------|
| Substitute for Form 1449/A/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary) | | | | Complete if Known | |
| | | | | Application No. | 10/077,142 |
| | | | | Filing Date | 02/15/2002 |
| | | | | First Named Inventor | D'Amato et al. |
| | | | | Group Art Unit | 1616 |
| Sheet 8 of 15 | | | | Examiner Name | Badio, Barbara P. |
| | | | | Attorney Docket Number | 05213-3000 (43170-269288) |
| OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS | | | | | |
| Examiner Initials | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published | | | T ² |
| | 42 | Author: GASLINI et al. Title: Reaction of Eugenol with Synthesis Gas. Synthesis of 5,6,7,8-Tetrahydro-3-methoxy-2-naphthol Publ: Journal of Organic Chemistry Vol/Iss: 29 (5) Pages: 1177-1180 Date: 05/1964 | | | |
| | 43 | Author: GIMBRONE, M.A. et al. Title: Tumor Growth and Neovascularization: An Experimental Model Using the Rabbit Cornea Publ: Journal of the National Cancer Institute Vol/Iss: 52(2) Pages: 413-427 Date: 02/74 | | | |
| | 44 | Author: GIMBRONE, M.A. et al. Title: Tumor dormancy <i>in vivo</i> by Prevention of Neovascularization Publ: Journal of Experimental Medicine Vol/Iss: 136 Pages: 261-276 Date: 1972 | | | |
| | 45 | Author: GONZALEZ et al. Title: Synthesis and Pharmacological Evaluation of 8 α Estradiol Derivatives Publ: Steroids Vol/Iss: 40 (2) Pages: 171-187 Date: 9/1982 | | | |
| | 46 | Author: GROSS, J.L. et al. Title: Modulation of Solid Tumor Growth <i>in vivo</i> by bFGF (Abstract only) Publ: Proceedings of the American Association of Cancer Research Vol/Iss: 31 Pages: 79 Date: 03/90 | | | |
| | 47 | Author: GUNZLER, V. Title: Thalidomide-A Therapy for the Immunological Consequences of HIV Infection? Publ: Medical Hypothesis Vol/Iss: 30 (2) Pages: 105-109 Date: 10/89 | | | |
| | 48 | Author: GUPTA et al. Title: Antifertility Agents. XIV. Secosteroids. VII. Synthesis of 2 α and 2 β , 6 β -dimethyl- 3 β -(p-hydroxyphenyl)-trans-bicyclo[4.3.0]nonan-7-ones and some related compounds (Abstract only) Publ: Indian Journal of Chemistry Vol/Iss: 13 (7) Pages: 759-760 Date: 1975 | | | |

| | |
|--------------------|-----------------|
| Examiner Signature | Date Considered |
|--------------------|-----------------|

¹Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language translation is attached.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

| | | | | | |
|---|----------|--|----|------------------------|---------------------------|
| Substitute for Form 1449/A/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary) | | | | Complete if Known | |
| | | | | Application No. | 10/077,142 |
| | | | | Filing Date | 02/15/2002 |
| | | | | First Named Inventor | D'Amato et al. |
| | | | | Group Art Unit | 1616 |
| | | | | Examiner Name | Badio, Barbara P. |
| | | | | Attorney Docket Number | 05213-3000 (43170-269288) |
| Sheet | 9 | of | 15 | | |
| OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS | | | | | |
| Examiner Initials | Cite No. | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published | | | |
| | 49 | Author: GUPTA et al. Title: Studies in Antifertility Agents. Part XVIII. 2α,6β-Diethyl-3β-(p-hydroxyphenyl)-trans-bicyclo[4.3.0]nonan-7β-ol and 6β-methyl-3β-(p-hydroxyphenyl)-2α-propyl- trans-bicyclo[4.3.0]nonan-7β-ol (Abstract only) Publi: Indian Journal of Chemistry Vol/Iss: 19B (10) Pages: 886-890 Date: 1980 | | | |
| | 50 | Author: GUTIERREZ-RODRIGUEZ et al. Title: Treatment of Refractory Rheumatoid Arthritis - The Thalidomide Experience Publi: The Journal of Rheumatology Vol/Iss: 16 (2) Pages: 158-163 Date: 02/89 | | | |
| | 51 | Author: GUTIERREZ-RODRIGUEZ, O. Title: Thalidomide - A Promising New Treatment for Rheumatoid Arthritis Publi: Arthritis and Rheumatism Vol/Iss: 27 (10) Pages: 1118-1121 Date: 10/84 | | | |
| | 52 | Author: HAHNEL et al. Title: THE SPECIFICITY OF THE ESTROGEN RECEPTOR OF HUMAN UTERUS Publi: Journal of Steroid Biochemistry Vol/Iss: 4 Pages: 21-31 Date: 1973 | | | |
| | 53 | Author: HANDLEY et al. Title: Chronic bullous disease of childhood and ulcerative colitis Publi: British Journal of Dermatology Vol/Iss: 127 (40) Pages: 67-68 Date: 07/01/92 | | | |
| | 54 | Author: HENEY et al. Title: Thalidomide treatment for chronic graft-versus-host disease Publi: British Journal of Haematology Vol/Iss: 78 (1) Pages: 23-27 Date: 05/91 | | | |
| | 55 | Author: HOLKER et al. Title: The Reactions of Estrogens with Benzeneseleninic Anhydride and Hexamethyldisilazane Publi: J. Chem. Soc. Perkin Trans. Vol/Iss: 1 Pages: 1915-1918 Date: 1982 | | | |

| | | | |
|--------------------|--|-----------------|--|
| Examiner Signature | | Date Considered | |
|--------------------|--|-----------------|--|

'Unique citation designation number. 'See attached Kinds of U.S. Patent Documents. 'Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 'For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 'Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. 'Applicant is to place a check mark here if English language translation is attached.

| | | | | | |
|---|-----------------------|---|----|------------------------|---------------------------|
| Substitute for Form 1449/A/PTO | | | | Complete if Known | |
| INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary) | | | | Application No. | 10/077,142 |
| | | | | Filing Date | 02/15/2002 |
| | | | | First Named Inventor | D'Amato et al. |
| | | | | Group Art Unit | 1616 |
| | | | | Examiner Name | Badio, Barbara P. |
| Sheet | 10 | of | 15 | Attorney Docket Number | 05213-3000 (43170-269288) |
| OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS | | | | | |
| Examiner Initials | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published | | | T ² |
| | 56 | Author: HORI, A. et al. Title: Suppression of Solid Tumor Growth by Immunoneutralizing Monoclonal Antibody Against Human Basic Fibroblasts Growth Factor Publ: Cancer Research Vol/Iss: 51 Pages: 6180-6184 Date: 11/15/91 | | | |
| | 57 | Author: IMAMURA et al. Title: Method for Manufacture of Dihydric Phenols (Abstract only) Publ: USPATEFULL 76:20259 US 3,950,437 Vol/Iss: Pages: Date: 04/13/1976 | | | |
| | 58 | Author: INGBER, D. et al. Title: Synthetic analogues of fumagillin that inhibit angiogenesis and suppress tumor growth Publ: Nature Vol/Iss: 348 Pages: 555-557 Date: 12/06/90 | | | |
| | 59 | Author: IRIARTE et al. Title: Steroids (XCIV). Synthesis of 2-methyl and 1,2-dimethyl estrogens (Abstract only) Publ: Tetrahedron Vol/Iss: 3 Pages: 28-36 Date: 1958 | | | |
| | 60 | Author: JHINGRAN et al. Title: Studies in Antifertility Agents - Part XLI: Secosteroids-x: Syntheses of Various Stereoisomers of (+)-2,6β-diethyl-7α-ethynyl-3-(p-hydroxyphenyl)-trans-bicyclo [4.3.0]nonan-7β-ol. Publ: Steroids Vol/Iss: 42 (6) Pages: 627-634 Date: 1983 | | | |
| | 61 | Author: KARWAT Title: Separation and Recovery of Hydrogen Sulfide from Hydrocarbon Mixture Publ: Carplus DE 1103310 Vol/Iss: Pages: Date: 09/02/1959 | | | |
| | 62 | Author: KIM, K.J. et al. Title: Inhibition of Vascular Endothelial Growth Factor-induced Angiogenesis Suppresses Tumor Growth In Vivo Publ: Nature Vol/Iss: 362 Pages: 841-844 Date: 04/29/93 | | | |

| | |
|--------------------|-----------------|
| Examiner Signature | Date Considered |
|--------------------|-----------------|

¹Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check-mark here if English language translation is attached.